Remarks

The above Amendments and these Remarks are in reply to the Final Office Action mailed 16 August 2006, and in further response to the telephone interview on December 5, 2006 with Examiner Cobanoglu and Primary Examiner Porter. The Examiners are thanked for the courtesy of their interview. Applicants believe that the claim amendments and remarks made herein are consistent with that interview.

Claims 1-51 were pending in the Application prior to the outstanding Office Action. In the Office Action, the Examiner rejected claims 1-51. The present Response amends claims 1, 6, 7, 10, 19, 20, 31-34, 38-44, 48 and 49, leaving for the Examiner's present consideration claims 1-51. Reconsideration of the rejections is requested.

On October 13, 2006 Applicants filed a Response B Under 37 CFR 1.116. This was followed by an Advisory Action mailed 03 November 2006, which did NOT enter Response B. The present Response C assumes that Response B was, and remains, NOT ENTERED.

I.   CLAIM REJECTIONS - 35 USC 112

The Examiner is thanked for the withdrawal in the Final Office Action of the rejections of claims 39 and 41 under 35 U.S.C. §112. In the Final Office Action, the Examiner has now rejected claims 1, 10 and 42 for indefiniteness.

      A.   Paragraph 2.B Rejection

            1.   "said protocol specification specifies such a parameter too vaguely to be encoded into said database"

In Paragraph 2.B of the Final Office Action, it is believed that the Examiner feels that the limits of the following claim language in claims 1, 10 and 42: "said protocol specification specifies such a parameter too vaguely to be encoded into said database", are too vague to satisfy the definiteness requirement of Section 112.

During the December 5, 2006 telephone interview the Examiners clarified that this language was considered indefinite because too much human judgment was called for to determine whether a parameter is specified in the protocol specification "too vaguely". The Examiners suggested that a reference in the claim to a slot in the database might be appropriate.

Applicants respectfully disagree that any human judgment required by this claim limitation rises to the level of indefiniteness, since the claim calls for "vagueness" to be measured by the capability of the database, not by a human. Nevertheless, Applicants have now revised each of claims 1, 10 and 42 to recite instead, "said protocol specification specifies such a parameter ~~too vaguely to be encoded into said database~~ with less precision than is required by a slot in said database for encoding the parameter." Applicants respectfully submit that any reliance on human judgment is avoided by this formulation.

A similar amendment has been made in independent claim 34.

2.   " said protocol specification specifies a such a parameter inconsistently "

Also in Paragraph 2.B of the Final Office Action, it is believed that the Examiner feels that the limits of the following claim language in claims 1, 10 and 42: "said protocol specification specifies a such a parameter inconsistently", are too vague to satisfy the definiteness requirement of Section 112.

Again the December 5, 2006 telephone interview the Examiners clarified that this language was considered indefinite because too much human judgment was called for to determine whether a parameter is specified in the protocol specification "inconsistently". The Examiners suggested that the claim could be amended using a word like "conflicting".

Again, Applicants respectfully disagree that the word "inconsistent" requires human judgment; Applicants believe that "inconsistency" can be determined in an entirely objective manner. Nevertheless, in accordance with the Examiners' suggestion, Applicants have amended each of claims 1, 10 and 42 to recite instead, "said protocol specification ~~specifies such a parameter inconsistently~~ contains at least two such parameter specifications which are in conflict." Applicants respectfully submit that any reliance on human judgment is avoided by this formulation.

A similar amendment has been made in independent claim 34.

B.   Paragraph 2.C Rejection

In paragraph 2.C of the Office Action, the Examiner says there is insufficient antecedent basis for the phrase "an indication that said operational uncertainty exists", in claims 1 and 42.

In their Response B Under 37 CFR 1.116, Applicants disagreed and pointed out that the "operational uncertainty" referred to in the step of encoding, was properly introduced earlier in the claim, specifically in the step of identifying.

The rejection was not mentioned again in the Advisory Action, nor was it raised again by the Examiners during the December 5, 2006 telephone interview. Applicants therefore believe that this rejection has been overcome.

C.   Encoding and Identifying Steps

Though not raised previously in any Office Action, the Examiners during the December 5, 2006 telephone interview raised an additional ground for indefiniteness. In particular, the Examiners noted that several of the claims call for a step of "encoding ... workflow tasks", and another step of "during said step of encoding, identifying an operational uncertainty" that for various reasons cannot be encoded into "said database". The Examiners took the position that if the operational uncertainty can't be encoded, then a step of "identifying" the operational uncertainty cannot take place "during said step of encoding".

Applicants pointed out that the above logical inconsistency forces a different construction of the claim language, specifically that the "step of encoding" should be interpreted to take place over a period of time, and not all of that time is spent actually writing data into the database. The step of "identifying an operational uncertainty" can take place "during" the overall step of encoding, without having to take place while actually writing data into the database. The Examiners did not respond to this point during the interview, leaving the undersigned with the impression that they would further consider this point when repeated by Applicants in the present Response C.

In order to emphasize the above interpretation, Applicants have now amended each of claims 1, 34 and 42 to call explicitly for the step of encoding workflow tasks into a database, to include "substeps of writing" information from the protocol specification into the database, and to call for the step of identifying an operational uncertainty to occur "during said step of encoding workflow tasks but not during any of said substeps".

Applicants believe that this was the interpretation required by the claim language as previously written, so Applicants believe that the scope of the claim has not been narrowed by this amendment. Regardless, however, it is respectfully submitted that this indefiniteness

objection raised by the Examiners during the December 5, 2006 telephone interview has been overcome.

II.   CLAIM REJECTIONS - 35 USC 103

A.   Paragraph 4.A Rejection: claims 1-9 and 42-51

The Examiner has rejected claims 1-9 and 42-51 under 35 U.S.C. §103(a) as being unpatentable over a combination of Brown, Friedman and Herren.

Applicants responded to these rejections in their un-entered Response B Under 37 CFR 1.116, but it does not appear from the Advisory Action that the Examiner was able to consider Applicants' points thoroughly. In particular, the Examiner's comments in the Advisory Action appear to rely again on the extraordinarily broad interpretation of the term "operational uncertainty" that the Examiner had used in the first Office Action. The Advisory Action recalls that in an earlier March 2, 2006 telephone interview the Examiner and her supervisor had suggested that Applicants cite a definition of the term from the specification, and again invites Applicants to do so. The Advisory Action appears to neglect that Applicants (in Response A) *did* respond to the Examiners' suggestion by amending to clarify the meaning of "operational uncertainty", just as suggested.

During the December 5, 2006 telephone interview, Applicants asked whether the Examiner might simply have forgotten about the citations and claim amendments made in Applicants' Response A. Without responding to this question specifically, the Examiner suggested that Applicants should re-submit their points from Response B and they will be considered. Accordingly, the remarks below are copied from Response B, revised slightly in light of the December 5, 2006 telephone interview.

1.   Independent Claim 1

The Examiner previously rejected claim 1 over a combination of only Brown and Friedman. Applicants responded (in Response A) with extensive claim amendments and remarks, mostly in response to the telephone interview conducted with the undersigned by the Examiner and her supervisor on March 2, 2006. In particular, Applicants not only directed the Examiner's attention to paragraph [0104] of Applicants' specification, which (among other

places) describes the term "operational uncertainty" in detail, but Applicants also amended the claim to incorporate language from the specification description directly into the claim.

In the Final Office Action the Examiner did not explain why Applicants' amendments and remarks were insufficient, but instead, merely added Herren to the combination.

Since the Examiner merely repeats many of the positions she took in the first Office Action, Applicants hereby incorporate by reference their comments from their Response A. In addition, Applicants particularly disagree with the Examiner's interpretation of Herren.

The Examiner points to Herren, col. 5, line 45 - col. 6, line 5 as teaching the following feature called for in Applicants' claim 1:

> ... identifying an operational uncertainty in which said protocol specification contains at least one of the following deficiencies: said protocol specification fails to specify a particular parameter for use during protocol execution, or said protocol specification specifies such a parameter too vaguely to be encoded into said database, or said protocol specification specifies such a parameter inconsistently.

But the cited paragraph of Herren contains no such teaching.

First, Herren teaches a system to help users design clinical trials by helping them to "effectively identify attributes for inclusion in a clinical trial, and attributes which are not useful to test." Clearly this takes place before a protocol specification has been drafted.

Thus this teaching *cannot* satisfy Applicants' claim elements calling for identifying an operational uncertainty in which said protocol specification contains a deficiency in which said protocol specification fails to specify a particular parameter for use during protocol execution, or said protocol specification specifies such a parameter with less precision than is required by a slot in said database, or said protocol specification specifies such a parameter in a conflicting manner.

"Said protocol specification" does not exist before a protocol specification has been drafted.

Accordingly, it is respectfully submitted that since none of the three references cited by the Examiner teaches this element of Applicants' claim, calling for a step of identifying an operational uncertainty in which "said" protocol specification contains a deficiency...., the combination of such references cannot render Applicants' claim obvious.

Second, Applicants submit that the Examiner is again misinterpreting the phrase "operational uncertainty" in Applicants' claim. As Applicants pointed out in the Examiner interview of March 2, 2006, the term "*operational* uncertainty" is explicitly distinguished in Applicants' specification from the term "*scientific* uncertainty". As defined therein:

> "A *scientific* issue arises due to the limited state of current knowledge about the trial agent(s) pharmacologic and therapeutic properties in the experimental clinical situation. This lack of scientific knowledge is precisely the reason a well-designed clinical trial is required. Scientific issues are ethically justified and do not indicate any problem with the clinical trial protocol. *Operational* issues arise because of unforeseen difficulties in executing the trial within the strict parameters or assumptions embedded implicitly or explicitly within the protocol design. In this case, the protocol designers may not have been able to predict the difficulties the field organization or clinical investigators may have in operationalizing specific study design components." Specification, paragraph [0025].

The issues addressed in the cited paragraph of Herren are clearly *scientific* issues, not *operational* issues. They arise because the designer does not yet know which attributes should or should not be tested in a clinical trial, not because an existing clinical trial protocol contains field organizational problems or because clinical investigators (i.e. those actually conducting the study in the field) cannot determine from the protocol what they are supposed to do during a particular patient visit.

During the December 5, 2006 telephone interview, the Examiner pointed to Herren's recitation that "In this manner, the user can determine the impact of various clinical trial designs prior to actual implementation of the clinical trial, to determine the likelihood of useful results." Herren, col. 5, lines 62-65. The Examiner argued that the phrase "various clinical trial designs" can include such design variations as how many patient visits to include, which would be an operational issue rather than a scientific issue.

But that is not the sense in which Herren is using the phrase. *In context*, Herren is clearly using the phrase with reference to design variations intended to address different *scientific* issues, not operational issues. The entire paragraph in which it appears is all about scientific issues:

- "the present invention ... helps researchers to develop information about the effects of a proposed intervention at the biological level (e.g., what patient types exhibit the best response to which form of intervention)." The issue of which

patient types exhibit the best response to a medical procedure is a *scientific* uncertainty, not an operational uncertainty. It is a scientific question that the study is designed to answer.

- "The present invention enables researchers to evaluate how patient attributes affect the impact of the intervention at the biological level." Again, this is a *scientific* question to be answered by a clinical trial, not an operational uncertainty that could impair the operation of a clinical trial.

- "The biological information is used to develop a proposed clinical trial design in terms of the patient types that should be included in a clinical trial and the attributes of the patient or intervention that need to be controlled for in the clinical trial design." The question of which biological or intervention factors need to be controlled for in the study (i.e., which factors need to be removed as possible alternative scientific reasons for the results obtained during the study), is a *scientific* question, not an "operational uncertainty" like an omitted, imprecise or conflicting statement of the number of visits that a patient is to make to the clinic.

- "More particularly, the present invention enables the user ... to determine which combinations of parameters and attributes are demonstrative of the efficacy of the intervention." Efficacy (i.e., whether the drug or medical procedure actually works), is a *scientific* question that the clinical trial is to test, not an operational uncertainty in the design of a clinical trial.

- "In contrast, in conventional clinical trial design, the biological parameters, patient attributes and intervention attributes are assumed, instead of being analyzed as part of the clinical trial design itself." Again, Herren here is talking about *scientific* aspects of the clinical trial design, not operational aspects.

- "By providing a data driven exploration of the alternative clinical trial design factors, the present invention enables a user to effectively identify attributes for inclusion in a clinical trial, and attributes which are not useful to test." The identification of attributes for testing is squarely a scientific question, not an operational question.

Thus there is no way that Herren's recitation that the "various clinical trial designs" referred to Herren in the middle of this paragraph which is all about how to choose a clinical trial design to best test *scientific* questions, would be interpreted by a person of ordinary skill to teach a step of "identifying an *operational* uncertainty" in which "said protocol specification" contains certain types of deficiencies.

Accordingly, Herren fails to teach the limitation in Applicant's claim calling for the step of "identifying an operational uncertainty". Again, since none of the three references cited by the Examiner teaches this element of Applicants' claim, the combination of such references cannot render Applicants' claim obvious.

Third, the Examiner appears to be ignoring the words in Applicants' claim language calling for the operational uncertainty to constitute at least one of three specific types of deficiencies. As amended herein, these listed types of deficiencies are: (1) "said protocol specification fails to specify a particular parameter for use during protocol execution", or (2) "said protocol specification specifies such a parameter with less precision than is required by a slot in said database for encoding the parameter," or (3) "said protocol specification contains at least two such parameter specifications which are in conflict."

If the Examiner believes that the Herren paragraph teaches identifying an operational uncertainty in which a "protocol specification fails to specify a particular parameter for use during protocol execution," it is respectfully requested that the Examiner point out where Herren teaches this.

Similarly, if the Examiner believes that the Herren paragraph teaches identifying an operational uncertainty in which a "protocol specification specifies such a parameter with less precision than is required by a slot" in the database in which the protocol specification is to be encoded, then it is again requested that the Examiner point out where Herren speaks of such a database, where he speaks of encoding into such a database, and where he compares the precision with which a parameter being encoded into such a database is specified in a protocol specification to the precision required by a slot in the database.

And again, if the Examiner believes that the Herren paragraph teaches identifying a deficiency in which a "protocol specification contains at least two such parameter specifications which are in conflict", then it is again requested that the Examiner point out where Herren speaks

of a parameter or parameters that are specified in two different places in a protocol specification, and in a conflicting manner.

Applicants respectfully see nothing in the paragraph cited by the Examiner that says anything about any of these three types of deficiencies.

Accordingly, Herren fails to teach the limitation in Applicant's claim calling for the step of identifying at least one of the three specified types of deficiencies. Yet again, therefore, since none of the three references cited by the Examiner teaches this element of Applicants' claim, the combination of such references cannot render Applicants' claim obvious.

To the extent the Examiner still believes that a step of identifying an operational uncertainty is taught in *Brown*, Applicants again respectfully point out that she is interpreting the term "operational uncertainty" much too broadly. The PTO's principle of giving claim terms their "broadest reasonable interpretation" does not give the Examiner unfettered discretion to ignore the usage of the terms in the specification. As pointed out in MPEP 2111, "The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach" in light of the specification. (citing In re Cortright, 165 F.3d 1353, 1359 (Fed. Cir. 1999), in which the Federal Circuit reversed the Board's construction of a claim limitation based on applicant's disclosure and other published examples of usage). Thus it is important for the Examiner tie the meaning of "operational uncertainty" to how the term would be understood by those of skill in the art in light of the specification.

Applicants' specification paragraph [0104] (for example) gives meaning to the phrase "operational uncertainty":

> [0104] As used herein, "operational uncertainties" include parameters that are either specified inconsistently in the text-based protocol, or specified only vaguely, or omitted altogether. Some parameters in a clinical trial protocol are left uncertain intentionally, and a well-designed database model will accommodate this level of uncertainty. For example, the temporal constraint from one protocol event to another may be specified in the text-based protocol as a permissible range of time periods, or as minimum, maximum and base time periods, or as a probability function. These may constitute "operational uncertainties" with respect to a simple database model that requires entry of only a single precise time period, but not with respect to more sophisticated database models that allow entry of the temporal constraint parameters in the form provided in the text. As another example, protocol specifications that intentionally allow some discretion on the part of the physician, are not necessarily "operational uncertainties". Thus an uncertainty is not considered an "operational uncertainty" unless the protocol specifies the parameter either

with unintentional ambiguity, or not at all, or with sufficient unintentional uncertainty that it cannot be encoded into the database without additional information from the provider of the protocol.

This specification language cannot be ignored when giving the claim phrase "operational uncertainty" its broadest reasonable interpretation.

Furthermore, as mentioned above even if the term "operational uncertainty" is given no patentable weight at all, Applicants' Response A incorporated limitations directly into the claim calling for identifying an uncertainty of any of three specified types. Nothing in any of the references cited by the Examiner teaches or suggests identifying an uncertainty of any of the three types specified in Applicants' claim. Certainly nothing in Brown or Herren teaches or suggests identifying such an uncertainty in the protocol specification.

For at least the reasons set forth above, in addition to the points that Applicants already made previously with respect to the Examiner's original proposed combination of Brown and Friedman, Applicants respectfully submit that the combination of Brown, Friedman and Herren cannot render Applicants' claim 1 obvious. Claim 1 therefore should be patentable.

2. <u>Dependent Claims 2-9</u>

The Examiner rejected claims 2-9 as being obvious over the combination of Brown, Friedman and Herren.

These claims all depend ultimately from independent claim 1 and therefore are believed to be patentable for at least the reasons set forth above with respect to independent claim 1. In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right.

<u>Claim 3</u>, for example, adds a limitation that the protocol specification objects into which certain workflow tasks called for in the clinical trial protocol specification not yet in execution are to be encoded, include "protocol event objects describing protocol events", and "temporal constraint objects describing temporal constraints among said protocol event objects".

The Examiner argues (in the rejection incorporated from the first Office Action) that these limitations are taught in Brown, col.6, lines 58-60 and col.7, lines 1-5. But these excerpts of Brown do not appear to say anything at all about protocol event objects describing protocol

events, or temporal constraint objects describing temporal constraints among said protocol event objects.

With regard to Applicants' limitation calling for temporal constraint objects describing temporal constraints among said protocol event objects, Applicants understand that the Examiner believes that temporal constraints are inherent in Brown because a clinical trial is always concerned with the progression of an illness or other condition over time. As an example, the Examiner has suggested that a clinical trial might include a question, to be asked of a patient, such as "How did you feel 6 hours after you took the pill?"

But not all clinical trials include such a hypothetical question. Inherency requires that the allegedly inherent teaching *necessarily* flows from the teachings of the applied prior art (MPEP 2112(IV)), which is clearly not the case as regards Brown. As requested in Applicants' Response A, if the Examiner wishes to make an inherency argument, then Applicants respectfully request that she do so with the full rigor required under MPEP 2112(IV). Otherwise, it is respectfully submitted that she has not made a prima facie case that anything in Brown teaches the limitations of Applicants' claim 3.

Additionally, the claim calls for the protocol specification objects to include "temporal constraint objects describing temporal constraints" among "protocol event objects".

Thus in order for the 6 hour time period in the Examiner's example question to satisfy the limitations of Applicants' claim, the time period would have to be specified by the protocol specification to occur between "protocol events", and it would have to be specified as a temporal constraint between such protocol events. An example is a protocol specification that the patient is to be called back for a next office visit 6 days after the previous office visit, where each of the visits are specified in "protocol event objects", and the 6-day time period is specified in a "temporal constraint object". The 6 hour time period in the Examiner's example question does *not* satisfy the literal limitations of Applicants' claim unless (1) both the taking of the pill and the patient's noting how he or she feels, are both specified by the protocol specification; (2) both events are described in "protocol event objects" as events that are to occur; (3) the protocol specification specifies that 6 hours are to elapse between the two events; and (4) the 6-hour time period is described in a "temporal constraint object" relating the two events together.

While a protocol specification could conceivably be encoded in this manner, Applicants respectfully submit that nothing in Brown suggests or makes it inherent that Brown has done so.

It is not at all clear from Brown that all of these conditions *necessarily* flow from the teachings of Brown.

Accordingly, it is respectfully submitted that claim 3 should be patentable in its own right.

Claims 6-9, as other examples, specify individual types of operational uncertainties that are to be identified in parent claim 1's step of "identifying an operational uncertainty".

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col.4, lines 15-19, as teaching a step of identifying all of these types of operational uncertainties. But that language of Brown says only that:

> "the subject is presented with narrowly structured questions and suggested answers provided by the protocol. The set of possible answers is restricted. In the event that a suggested answer is ambiguous, inapplicable or raises new questions, a protocol can present a new question to the subject. This elimination of fuzzy answers imposes a logical structure upon the subjects' assessments."

First, this excerpt does not refer to operational uncertainties in the protocol specification. In fact it evidences a well-designed protocol specification, since the specification appears to be pre-designed to present a new question if the subject's answer is ambiguous, inapplicable or raises new questions.

Second, claims 6-9 refer to specific types of operational uncertainties: conflicting parameters in the protocol specification (claim 6), a parameter specified in the protocol specification with insufficient precision (claim 7), an omitted parameter in the protocol specification (claim 8), and a temporal constraint among at least two protocol events which, according to parent claim 1, are specified by the protocol to occur during execution of the protocol (claim 9).

A "fuzzy answer" by the subject constitutes none of these.

Accordingly, dependent claims 2-9 are believed to be patentable.

B.   Claims 10-22

1.   Independent Claim 10

The Examiner rejected claim 10 as being obvious over a combination of Brown, Cunningham and Herren.

Claim 10 has been amended to call for, among other things, a database that includes:

a disambiguation comment object which identifies an operational uncertainty in which said protocol specification contains at least one of the following deficiencies: said protocol specification fails to specify a particular parameter for use during protocol execution, or said protocol specification specifies such a parameter with less precision than is required by a slot in said database for encoding the parameter, or said protocol specification contains at least two such parameter specifications which are in conflict, said disambiguation comment object being associated with at least a particular one of said objects in said database.

The Examiner cites Brown as teaching this limitation, and cites Herren as supporting "the obviousness of modifying the teaching of Brown and Cunningham to include protocol specification specifies to occur during execution of said protocol (as taught by Herren) is as addressed above in the rejection of claim 1 and incorporated herein." (emphasis in original)

But as pointed out in Applicants' Response A with respect to claim 1, Brown neither teaches nor suggests that his database include an object which identifies an "operational uncertainty" in which the protocol specification contains any of the three specific types of deficiencies called for in the claim.

Nor do Applicants understand how Herren supports the obviousness of modifying Brown's teachings to "include protocol specification specifies to occur during execution of said protocol". As pointed out above with respect to claim 1, the cited paragraph of Herren teaches only certain steps that take place before a protocol specification is even drafted, and therefore cannot teach anything about operational uncertainties in which "said protocol specification" contains deficiencies.

Accordingly, it is respectfully submitted that independent claim 10 should be patentable.

2.   Dependent Claims 11-22

The Examiner rejected claims 11-22 as being obvious over the combination of Brown, Cunningham and Herren.

These claims all depend ultimately from independent claim 10 and therefore are believed to be patentable for at least the reasons set forth above with respect to independent claim 10. In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right.

Claim 12, for example, adds a limitation that the protocol specification objects in the machine readable database, include "protocol event objects describing protocol events", and "temporal constraint objects describing temporal constraints among said protocol event objects".

The Examiner makes (in the incorporated first Office Action) the same citation to Brown, col. 6, lines 58-60 and col. 7, lines 1-5, that she made with respect to claim 3. Applicants therefore incorporate their response as set forth above with respect to claim 3.

Claim 14, which depends from claim 12, adds a limitation that the disambiguation comment object, which according to claim 10 identifies an operational uncertainty, be associated with a particular one of the temporal constraint objects introduced in claim 12.

The Examiner cites (in the incorporated first Office Action) Brown, col.6, lines 58-60 and col.7, lines 1-5 as teaching this limitation, but these excerpts of Brown do not appear to say anything at all about "disambiguation comment objects", "temporal constraint objects", and associations between them.

Claim 15, which depends from claim 14, adds a limitation that the operational uncertainty concern the amount of time allowed to elapse between two protocol events identified by the particular temporal constraint object introduced in claim 14.

The Examiner cites (in the incorporated first Office Action) Brown, col.3, lines 49-60 as teaching this limitation.

This section of Brown says:

> For example, it would be advantageous to provide a device [that allows] researchers to (1) collect, analyze and respond to input from the research subjects or participants in real time, (2) evaluate fuzzy assessments made by a subject or participant by making progressively narrower inquiries designed to obtain specific data, (3) aggregate and analyze data from a large number of remote sites quickly, (4) change the research protocol in response to input from subjects in real time and (5) rapidly identify responders and non-responders by correlating the data with a number of disparate parameters that are not necessarily apparent when the study begins."

Nothing in this excerpt appears to say anything at all about an operational uncertainty concerning the amount of time allowed to elapse between two protocol events identified by a temporal constraint object, as called for in Applicants' claim.

Claim 18, which depends from claim 16, which depends in turn from claim 12, adds a limitation that the disambiguation comment object of claim 10 be associated with a workflow task object describing an event that the protocol specification specifies to occur during execution.

The Examiner cites (in the incorporated first Office Action) Brown, col.4, lines 15-19 as teaching this feature.

But this section of Brown says only that "In the event that a suggested answer is ambiguous, inapplicable or raises new questions, a protocol can present a new question to the subject. This elimination of fuzzy answers imposes a logical structure upon the subjects' assessments."

This language of Brown says nothing about a "disambiguation comment object", which according to parent claim 10 "identifies an operational uncertainty in which said protocol *specification* contains at least one of" the three specified types of deficiencies. As pointed out above with respect to claims 6-9, the cited excerpt of Brown reveals a well-designed protocol specification in which a potential operational uncertainty is *averted* by the ability to present new questions to a subject to clarify fuzzy answers. The potential problem was foreseen and handled in the protocol *specification*, so that it is no longer an "operational uncertainty". Brown does not teach a machine readable database which includes a disambiguation comment object identifying *any* "operational uncertainty" in the protocol specification.

Claims 19-22 specify individual types of operational uncertainties that are to be identified in parent claim 10's disambiguation comment object.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col.4, lines 15-19, as teaching disambiguation comment objects identifying all of these types of operational uncertainties. But as set forth above with respect to claims 6-9, that language of Brown does not refer to operational uncertainties in the protocol specification. It evidences the

opposite: a well-designed protocol specification apparently pre-designed to present a new question if the subject's answer is ambiguous, inapplicable or raises new questions.

Additionally, claims 19-22 refer to specific types of operational uncertainties: conflicting parameters in the protocol specification (claim 19), a parameter specified in the protocol specification with insufficient precision (claim 20), an omitted parameter in the protocol specification (claim 21), and the amount of time allowed to elapse between two of the protocol events (claim 22).

A "fuzzy answer" by the subject constitutes none of these.

Accordingly, dependent claims 11-22 are believed to be patentable.

C.   Claims 23-33

1.   Independent Claim 23

The Examiner rejected claim 23 as being obvious over the same combination of Brown, Cunningham and Herren. Specifically, the Examiner cites Brown, col. 3, line 66 to col. 4, line 19, and col. 3, lines 49-60, as teaching the claimed features.

Applicants amended claim 23 extensively in their Response A, and provided detailed remarks (hereby incorporated herein) explaining why the cited combination does not render the claim obvious. Briefly, Applicants pointed out that neither Brown nor Cunningham or suggest the use of a pre-specified class structure as called for in claim 23, and they certainly do not teach the use of such a pre-specified class structure to define "protocol event specification objects describing protocol events that a protocol specification specifies to occur during execution of said protocol".

Applicants also pointed out that nothing in Brown teaches or suggests a database that includes "temporal constraint specification objects describing temporal relationships that a protocol specification specifies to occur among protocol events described in said protocol event specification objects, at least a particular one of said temporal constraint specification objects identifying an amount of time that said protocol specifies is to elapse between two or more protocol events when the protocol is executed."

Nor is the Examiner's argument persuasive that temporal constraints are inherent in Brown because a clinical trial is always concerned with the progression of an illness or other

condition over time. In their Response A Applicants demanded support for this inherency position pursuant to MPEP 2112(IV), but the Examiner still has not provided it.

In the final Office action, the Examiner did not respond at all to Applicants' extensive claim revisions and remarks. The new rejection differs from that of the first Office action only in the addition of a short additional section of Brown (Brown, col. 4, lines 3-19), and the addition of Herren to the combination.

But the added section of Brown does not answer any of Applicants' remarks made in their Response A. It does not teach or suggest the use of a pre-specified class structure, does not teach or suggest the use of such a pre-specified class structure to define "protocol event specification objects describing protocol events that a protocol specification specifies to occur during execution of said protocol", does not teach or suggest a database that includes "temporal constraint specification objects" as called for in the claim, and does not provide any basis to support the Examiner's position that temporal constraints are "inherent" in Brown.

And the Examiner's addition of Herren to the combination also appears to be unhelpful, since the Examiner does not provide any information at all about what she believes Herren teaches with respect to claim 23.

Accordingly, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case that claim 23 is unpatentable.

2.   Dependent Claims 24-33

The Examiner rejected claims 24-33 as being obvious over the same combination of Brown, Cunningham and Herren.

These claims all depend ultimately from independent claim 23 and therefore are believed to be patentable for at least the reasons set forth above with respect to independent claim 23. In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right.

Claim 26, for example, adds a limitation that the "amount of time" identified in a "temporal constraint specification object" of parent claim 23, specifically describe "the time that a hypothetical patient is expected to take between protocol events" that are described in two identified ones of the "protocol event objects" of parent claim 23.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col. 3, lines 49-60 as teaching this feature. This section of Brown says:

> For example, it would be advantageous to provide a device [that allows] researchers to (1) collect, analyze and respond to input from the research subjects or participants in real time, (2) evaluate fuzzy assessments made by a subject or participant by making progressively narrower inquiries designed to obtain specific data, (3) aggregate and analyze data from a large number of remote sites quickly, (4) change the research protocol in response to input from subjects in real time and (5) rapidly identify responders and non-responders by correlating the data with a number of disparate parameters that are not necessarily apparent when the study begins."

Nothing in this excerpt appears to say anything at all about "the time that a hypothetical patient is expected to take between protocol events".

Claim 27, as another example, depends from claim 23 and adds a limitation that the particular temporal constraint object of claim 23, which identifies an amount of time specified by the protocol to elapse between protocol events when the protocol is executed, to identify such amount of time "by identifying at least one member of the group consisting of minimum and maximum times".

The Examiner (in the rejection incorporated from the first Office Action) again cites Brown, col. 3, lines 49-60 as teaching this feature.

But again, nothing in that excerpt appears to say anything at all about minimum or maximum times that the protocol specification prescribes to elapse between protocol events when the protocol is executed.

Claim 28, as yet another example, depends from claim 27 and adds a limitation that the particular temporal constraint object identify the amount of time by identifying *both* the minimum and maximum times.

The Examiner (in the rejection incorporated from the first Office Action) again cites Brown, col. 3, lines 49-60 as teaching this feature.

But again, nothing in that excerpt appears to say anything at all about minimum or maximum times that the protocol specification prescribes to elapse between protocol events when the protocol is executed.

Claim 29 depends from claim 28 and adds a limitation that the particular temporal constraint object identify the amount of time *further* by identifying a "base time" between the minimum and maximum times.

The Examiner (in the rejection incorporated from the first Office Action) again cites Brown, col. 3, lines 49-60 as teaching this feature.

But again, nothing in that excerpt appears to say anything at all about minimum, maximum or base times that the protocol specification prescribes to elapse between protocol events when the protocol is executed.

Claim 30 depends from claim 23 and adds a limitation that the plurality of machine readable objects in claim 23 further include a "disambiguation comment object" associated with the particular temporal constraint object, and that this disambiguation comment object identify an "operational uncertainty" in a particular temporal relationship identified in the temporal constraint object. Thus the claim addresses the concept of an "operational uncertainty" specifically in the "amount of time" that the protocol specifies is to elapse between two or more protocol events when the protocol is executed, and calls for this operational uncertainty to be identified in a "disambiguation comment object" associated with the particular "temporal constraint object" in which the "amount of time" is identified.

The Examiner cites Brown, col. 4, lines 15-17 as teaching this feature.

But that section of Brown says only that, "In the event that a suggested answer is ambiguous, inapplicable or raises new questions, a protocol can present a new question to the subject."

That language of Brown appears to have nothing to do with any "operational uncertainties" in "amounts of time" that the protocol specifies is to elapse between two or more protocol events when the protocol is executed. It certainly says nothing about such any "disambiguation comment object" identifying such an operational uncertainty, or any "temporal constraint object" in which the "amount of time" is identified, or that either be "associated" with the other.

Claims 31-32 have been amended to depend from claim 30, correcting typographical errors. These claims specify individual types of operational uncertainties that are to be identified in parent claim 30's disambiguation comment objects.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col.4, lines 15-17, as teaching both of these types of operational uncertainties. But that language of Brown says only that:

> " In the event that a suggested answer is ambiguous, inapplicable or raises new questions, a protocol can present a new question to the subject."

First, as pointed out above with respect to claims 6-9, this excerpt does not refer to operational uncertainties in the *protocol specification*. It evidences a well-designed protocol specification that is fully able to handle a subject's answer that is ambiguous, inapplicable or raises new questions.

Second, these claims refer to specific types of operational uncertainties: an inconsistency in a temporal relationship as specified in the protocol specification (claim 31), and vagueness in a temporal relationship as specified in the protocol specification (claim 32). An answer by a subject that is "ambiguous, inapplicable or raises new questions", received <u>during protocol execution,</u> constitutes neither of these.

<u>Claim 33</u> has also been amended to depend from claim 30, correcting a typographical error. This claim specifies that the operational uncertainty identified in claim 23's disambiguation comment object comprise an omission of a particular temporal relationship from the protocol specification.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col. 7, lines 1-5 as teaching this feature. That excerpt from Brown recites:

> "At a step 216, the medical research expert 121 review the updated information and protocol 131 and the other information input by the set of research subjects 111 and either leave the updated research information and protocol unchanged or modify it as necessary."

Again, there is nothing in this excerpt that refers to any disambiguation comment objects identifying an operational uncertainty specifically comprising an omission of a particular temporal relationship from the protocol specification, as called for in Applicants' claim.

Accordingly, claims 24-33 are believed to be patentable.

D.   Claims 34-41

1.   Independent Claim 34

The Examiner rejected claim 34 as being unpatentable over a combination of Brown, Friedman, Cunningham and Herren.

The Examiner states that claim 34 "disclose the same limitations of claim 23 and claim 1", and therefore rejected claim 34 on the same ground as claims 23 and 1.

Applicants respectfully disagree that claim 34 "disclose the same limitations of claim 23 and claim 1". Claim 34 is an independent claim that contains its own limitations.

Nor do claims 23 and 1 contain the same limitations as each other.

Claim 34 in fact calls for a combination of elements that are not combined in any other claim in the application. To the extent the Examiner's reference to claims 1 and 23 are intended to represent citations to prior art excerpts that the Examiner considers to teach the individual claim elements of claim 34, Applicants respectfully incorporate by reference the points they have made above and in Response A.

But even if that is how the Examiner intends her rejection to be interpreted, the rejection would thus constitute an assertion that it would obvious to combine the teachings that the Examiner applied to certain elements of claim 1 with the teachings that the Examiner applied to certain elements of claim 23. And the Examiner proposes making this combination without citing or identifying any motivation for the obviousness of combining these teachings to make the particular combination of elements and steps called for in claim 34.

Accordingly, it is respectfully submitted that the Examiner has failed even to make a *prima facie* case that claim 34 is unpatentable.

2.   Dependent Claims 35-41

The Examiner rejected dependent claims 35-41 as being obvious over the same combination of Brown, Friedman, Cunningham and Herren.

These claims all depend ultimately from independent claim 34 and therefore are believed to be patentable for at least the reasons set forth above with respect to independent claim 34. In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right.

Claim 37, for example, depends from claim 36 which depends in turn from claim 34. Claim 37 adds a limitation that the "protocol specification objects " into which slots of claim 34 are organized, include "protocol event objects" describing protocol events and "temporal constraint objects" describing temporal constraints among events described in the protocol event objects. Each of the temporal constraint objects further is to include at least one slot for identifying an "amount of time" allowed between two or more protocol events.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col.3, lines 49-60 as teaching these features.

But nothing in the cited excerpt appears to say anything at all about "temporal constraint objects" describing temporal constraints among protocol events, much less a slot in the temporal constraint objects for identifying an "amount of time" allowed between two or more protocol events.

Claim 38, which has been amended for conformity with its parent claim 37, is another example. Claim 38 and adds limitations calling for steps of "instantiating" a disambiguation data object describing an operational uncertainty, and "associating" this object with a "temporal constraint" object of parent claim 37.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col. 4, lines 15-19 and col. 3, lines 49-60 as teaching these features.

But neither excerpt from Brown says anything about "instantiating" a data object, especially one that describes an "operational uncertainty". Nor does either excerpt say anything about "associating" a data object that describes an operational uncertainty, with a "temporal constraint" object that includes a slot for identifying an "amount of time" allowed between two or more protocol events.

Claim 39, as another example, depends from claim 34 and specifies that the particular type of operational uncertainty to be identified in parent claim 34's step of "identifying an operational uncertainty" involve conflicting values in the protocol specification regarding a particular amount of time.

The Examiner cites Brown, col.4, lines 15-17 and col.3, lines 49-60 as teaching these limitations. But those excerpts, as pointed out elsewhere herein, do not appear to say anything

about identifying "a particular amount of time" as specified in the protocol specification as an "operational uncertainty".

Claim 40, as yet another example, depends from claim 34 and specifies that the particular type of operational uncertainty to be identified in parent claim 34's step of "identifying an operational uncertainty" be an "amount of time" specified by the protocol specification "with less precision than is required".

Again, note that such imprecision in an amount of time specified in the protocol specification is not objectionable unless it rises to the level of "an operational uncertainty" as called for in the claim.

As with claim 39, the Examiner cites Brown, col.4, lines 15-17 and col.3, lines 49-60 as teaching these limitations. But those excerpts, as pointed out elsewhere herein, do not appear to say anything about identifying imprecision in a particular amount of time as specified in the protocol specification as an "operational uncertainty".

Claim 41, as yet another example, depends from claim 34 and specifies that the particular type of operational uncertainty to be identified in parent claim 34's step of "identifying an operational uncertainty" be "omission" of a particular amount of time from the protocol specification.

The Examiner cites Brown; col.7, lines 1-5 and col.3, lines 15-17 as teaching these limitations. But those excerpts do not say anything about the *omission* of an particular amount of time from the protocol specification.

Accordingly, dependent claims 35-41 are believed to be patentable.

E.   Claims 42-51
         1.   Independent Claim 42
The Examiner rejected claim 42 on the same grounds as claim 1.

Applicants therefore incorporate their remarks above, regarding claim 1.

Claim 42 is believed to be patentable.

         2.   Dependent Claims 43-51

The Examiner rejected dependent claims 43-51 as being obvious for reasons incorporated from the first Office Action. Claims 43 and 44 have been amended to more clearly describe the aspects to which these claims are directed.

Claims 43-51 all depend ultimately from independent claim 42 and therefore are believed to be patentable for at least the reasons set forth above with respect to independent claim 42. In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right.

Claim 44, for example, adds a limitation, among other things, that the protocol specification objects into which certain workflow tasks called for in the clinical trial protocol specification not yet in execution are to be encoded, include "protocol event objects describing protocol events", and "temporal constraint objects describing temporal constraints among said protocol event objects".

The Examiner argues (in the rejection incorporated from the first Office Action) that these limitations are taught in Brown, col.6, lines 58-60 and col.7, lines 1-5. But as set forth above with respect to claim 3, these excerpts of Brown do not appear to say anything at all about protocol event objects describing protocol events, or temporal constraint objects describing temporal constraints among said protocol event objects.

Additionally, the claim calls for the protocol specification objects to include "temporal constraint objects describing temporal constraints" among "protocol event objects".

As explained above with respect to claim 3, finding this teaching in Brown requires the Examiner to make an inherency argument which she has not done.

Claims 48-51 add limitations specifying individual types of operational uncertainties that are to be identified in parent claim 42's step of encoding workflow tasks.

The Examiner (in the rejection incorporated from the first Office Action) cites Brown, col.4, lines 15-19, as teaching disambiguation comment objects identifying all of these types of operational uncertainties. But as set forth above with respect to claims 6-9 and 19-22, that language of Brown does not refer to operational uncertainties in the protocol specification. It evidences the opposite: a well-designed protocol specification apparently pre-designed to present a new question if the subject's answer is ambiguous, inapplicable or raises new questions.

Additionally, claims 48-51 refer to specific types of operational uncertainties: conflicting parameters in the protocol specification (claim 48), a parameter specified in the protocol specification with insufficient precision (claim 49), an omitted parameter in the protocol specification (claim 50), and a temporal constraint among at least two of the protocol events (claim 51).

A "fuzzy answer" by the subject, given during execution of the protocol, constitutes none of these.

Accordingly, claims 43-51 are believed to be patentable.

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III   CONCLUSION

The references cited by the Examiner but not relied upon have been reviewed, but are not believed to render the claims unpatentable, either singly or in combination.

In light of the above, it is respectfully submitted that all of the claims now pending in the subject patent application should be allowable, and a Notice of Allowance is requested. The Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting issuance of a patent.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-0869 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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